Potential use of stem cells as a therapy for cystinosis.

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Public Summary:
Cystinosis is an hereditary disease characterized by the accumulation of cystine in all the cells of the body leading to cell death and tissue degeneration such as kidneys, liver, eyes, muscle and brain. We showed that healthy hematopoietic stem cells (HSCs), which are naturally available in the body, can rescue this disease in the mouse model of cystinosis and we are currently developing a clinical trial that allows the patients' own stem cells to be isolated, corrected for the genetic defect and reintroduced in the patients to stimulate healing. This review report the overall preclinical data that support the clinical translation of the stem cell gene therapy approach for cystinosis and how HSPC transplantation could be an effective one-time treatment to treat cystinosis but also other LSDs associated with a lysosomal transmembrane protein dysfunction.

Scientific Abstract:
Cystinosis is an autosomal recessive metabolic disease that belongs to the family of lysosomal storage disorders (LSDs). Initial symptoms of cystinosis correspond to the renal Fanconi syndrome. Patients then develop chronic kidney disease and multi-organ failure due to accumulation of cystine in all tissue compartments. LSDs are commonly characterized by a defective activity of lysosomal enzymes. Hematopoietic stem and progenitor cell (HSPC) transplantation is a treatment option for several LSDs based on the premise that their progeny will integrate in the affected tissues and secrete the functional enzyme, which will be recaptured by the surrounding deficient cells and restore physiological activity. However, in the case of cystinosis, the defective protein is a transmembrane lysosomal protein, cystinosin. Thus, cystinosin cannot be secreted, and yet, we showed that HSPC transplantation can rescue disease phenotype in the mouse model of cystinosis. In this review, we are describing a different mechanism by which HSPC-derived cells provide cystinosin to diseased cells within tissues, and how HSPC transplantation could be an effective one-time treatment to treat cystinosis but also other LSDs associated with a lysosomal transmembrane protein dysfunction.